

Serial No.: 09/927,160  
Filed: August 9, 2001

Please amend the application as follows to comply with requirements for patent applications containing nucleotide sequence and/or amino acid sequence disclosures in adherence with rules 37 C.F.R. § 1.821-1.825:

**IN THE SPECIFICATION:**

Please replace the paragraph beginning at page 14, line 5, with the following rewritten paragraph:

B<sup>1</sup> – Fig. 5. PCR products and primers (SEQ ID NOS:1-3) from the lacZ ( $\beta$ -galactosidase) gene sequence. The location of the 11 bp Xba linker (SEQ ID NO:4) is shown.–

Please replace the paragraph beginning at page 20, line 15, with the following rewritten paragraph:

B<sup>2</sup> – Figs. 20A and 20B. The organization of the mouse OTC gene. Sequence of cDNA probes and PCR primers used in this study are indicated (SEQ ID NO:5). Sizes of the exons in base pairs are indicated. The relative position of PCR primers M9, M8 and M11 are shown. B) Map of plasmid pTAOTC1. A 250 bp fragment containing the normal OTC exon 4 sequence and surrounding introns were cloned into the EcoRV site of pbluescript SK (+) (Stratagene).–

Please replace the paragraph beginning at page 20, line 21, with the following rewritten paragraph:

B<sup>3</sup> – Fig. 21. Sequence analysis of exon 4 of the mouse OTC gene in founder mice. PCR amplification of genomic DNA from tail biopsies of a pool of all of the homozygous

Serial No.: 09/927,160

Filed: August 9, 2001

B<sup>3</sup>  
(spf-ash/spf-ash) females used as egg donors and each indicated individual founder mice were sequenced using cycle sequencing with the M11 primer (Cyclist kit, Stratagene). The DNA sequence surrounding the spf-ash locus (arrow) in the OTC gene is shown (SEQ ID NO:6).—

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Please replace the paragraph beginning at page 69, line 1, with the following rewritten paragraph:

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B<sup>4</sup>  
— The plasmid pMC1lacpA (8.4 kb) contains the strong polyoma virus promoter of transcription plus ATG placed in front of the lacZ gene. The polyadenylation signal from SV40 virus was placed in back of the lacZ gene. The plasmid vector was pIB130 from IBI (New Haven, CT). The mutant vector pMC1lacpA has a 11-bp insertion in the XbaI site consisting of the inserted sequence CTCTAGACGCG (see Figure 5; SEQ ID NO:4).—

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Please replace the paragraph beginning at page 69, line 11, with the following rewritten paragraph:

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B<sup>5</sup>  
— We synthesized two 20-bp primers (PCR $\alpha$  and PCR $\beta$ ; SEQ ID NOS:2 &3) for producing a 276-bp PCR product (see Figure 5) from the wild-type lacZ sequence for use as targeting polynucleotides. We chose this 276-bp fragment to span the 11 bp insertion mutation as a nonhomologous sequence. The 276-bp DNA oligonucleotide was separated by gel electrophoresis and electroeluted from agarose, ethanol precipitated, and its concentration determined by absorbance at 260 nm. The 276-bp fragment was 5' end-

Serial No.: 09/927,160

Filed: August 9, 2001

$\beta^5$  labeled with  $^{32}\text{P}$  and specifically D-looped with the pMc1lacXpA or pMC1lacpA plasmid

DNA using recA as shown by agarose gel electrophoresis. -

Please replace the paragraph beginning at page 78, line 23, with the following rewritten paragraph:

$\beta^6$  - CF1 S 5'-GCAGAGTACCTGAAACAGGA (SEQ ID NO:7)-

Please replace the paragraph beginning at page 78, line 24, with the following rewritten paragraph:

$\beta^7$  - CF5 A 5'-CATTACAGTAGCTTACCCA (SEQ ID NO:8)-

Please replace the paragraph beginning at page 78, line 25, with the following rewritten paragraph:

$\beta^8$  - CF6 A 5'-CCACATATCACTATATGCATGC (SEQ ID NO:9)-

Please replace the paragraph beginning at page 78, line 28, with the following rewritten paragraph:

$\beta^9$  - CF17 S 5'-GAGGGATTGGGGAATTATTG (SEQ ID NO:10)-

Please replace the paragraph beginning at page 78, line 29, with the following rewritten paragraph:

$\beta^{10}$  - OLITGO N A 5'-CACCAAAGATGATATTTTC (SEQ ID NO:11)-

$\beta^{12-10-21}$  Please replace the paragraph beginning at page 80, line 1, with the following rewritten paragraph:

$\beta^{11}$  - OLIGO  $\Delta$ F A 5'-AACACCAAGATATTTTCTT (SEQ ID NO:12)-